#### REMARKS

Reconsideration is respectfully requested.

Claims 42-65 are pending. Claims 1-41 and 53 have been cancelled. Claim 65 has been withdrawn. Claims 42, 45, and 49 have been amended to include the limitations of claim 53. Claims 42-64 are under examination.

With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

### Finality of the Previous Office Action

Applicants thank the Examiner for withdrawing the finality of the previous Office Action, and withdrawing the grounds for rejection.

#### Election/Restriction

The Examiner has withdrawn claim 65 as directed to a constructively non-elected invention by original presentation. Applicants have amended claim 65 to include all limitations of the apparatus of claim 42. Upon allowance of claim 42, Applicants request rejoinder of claim 65. MPEP § 806.05(i).

## Claim Rejections - 35 U.S.C. §102

Claims 45-47, 53, 55-57 and 60-64 stand rejected under 35 U.S.C. §102(e) as anticipated by Lennox et al., U.S. Patent No. 6,461,490 ("Lennox") as defined by Morris C. ed (Academy Press Dictionary of science and Technology, Academic Press, San Diego, 1992, page 1726) ("Morris").

For an anticipation rejection under 35 U.S.C. §102 to be proper, a single reference must expressly or inherently disclose each and every element of a claim. In re Paulsen, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing Richardson v. Suzuki Motor Co., 9 USPQ2d

1913, 1920 (Fed. Cir. 1989). Lennox, as defined by Morris, fails to teach every limitation of the claimed invention.

Without acquiescing or admitting the Examiner's position, and solely to facilitate prosecution on the merits, Applicants have incorporated the limitations of claim 53 into independent claims 42, 45, and 49. Moreover, Applicants expressly traverse the definition of "printed circuit board" proffered by the Examiner.

Amended claims 42, 45, and 49 require the capture binding ligand "comprising a nucleic acid" to be "covalently attached to said electrode." The Examiner incorrectly asserts that "Lennox et al. disclose the biochip wherein the binding ligands [comprise] nucleic acids (Column 8, lines 38-41)." The "complementary nucleic acid strands" disclosed by Lennox et al. a) do not serve as "capture binding ligands," and b) a capture binding ligand comprising a nucleic acid is not covalently attached to the electrode.

The claims recite a capture binding ligand comprising a nucleic acid. Conversely, the capture binding ligand disclosed by Lennox et al. is an HSP1 protein, and does not comprise a nucleic acid. Lennox et al. further discloses that an HSP1 protein covalently attached to the substrate, and a nucleic acid-modified HSP2 protein that non-covalently binds to HSP1. The nucleic acid modification of HSP2 is therefore not covalently linked to the conductive film surface. As such, Lennox fails to describe a capture binding ligand comprising a nucleic acid, wherein the capture binding ligand is covalently attached to the electrode.

Because Lennox et al. fails to teach all claim limitations, Lennox et al. fails to anticipate the claimed invention. Applicants respectfully request that this ground for rejection be withdrawn.

## Claim Rejections – 35 U.S.C. §103

Claims 42-44, 46-58 and 60-64 stand rejected as unpatentable over Lennox in view of Anderson et al., US Patent No. 6,326,211 ("Anderson").

Claim 59 stands rejected over Lennox, as defined by Morris, in view of Anderson et al., and in further view of Hayes et al. (USSN 6,334,980).

35 U.S.C. § 103(a) requires that "differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains." 35 U.S.C. § 103(a). The prima facie case must satisfy three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior art combined with general knowledge must include a suggestion or incentive to modify or combine the references; and 3) the modification or combination must have a reasonable chance of success.

Applicants again traverse the definition of "printed circuit board" based on Morris.

1. The combined references fail to teach a "capture binding ligand comprising a nucleic acid, wherein the capture binding ligand is covalently attached to said electrode," as required by the claims.

As discussed above, The "complementary nucleic acid strands" disclosed by Lennox et al. a) do not serve as "capture binding ligands," and b) a capture binding ligand comprising a nucleic acid is not covalently attached to the electrode. Anderson fails to provide such a teaching; instead, Anderson describes conventional preparation of oligonucleotides arrays, not covalently attaching capture binding ligands that contain nucleic acids to an electrode. With respect to the rejection of claim 59, Hayes also fails to teach every limitation.

As such, the references as a whole fail to teach the claimed invention.

2. The cited references fail to provide the requisite motivation or suggestion to modify their teachings and supply the missing claim limitations.

In addition to failing to disclose every limitation of the rejected claims, the Lennox and Anderson references together fail to provide the requisite motivation or suggestion to alter their teachings to provide a capture binding ligand comprising a nucleic acid, wherein the capture binding ligand is covalently bound to an electrode. No teaching of the claimed subject matter is made in any of the cited references, and as such the cited references as a whole fail to provide the requisite motivation or suggestion to make the claimed invention.

3. Modifying the cited references to make the claimed invention would impermissibly change the principle of operation of the primary Lennox et al. reference.

A "proposed modification cannot change the principle of operation of a reference." MPEP § 2143.01. Moreover, "if a proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." MPEP § 2143.01.

In the present application, changing the HSP1 capture binding ligand to "a capture binding ligand comprising a nucleic acid" as claimed fundamentally changes the principle of operation of Lennox et al. The HSP1 - HSP2 non-covalent binding recited in Lennox et al. depends on the a repeated heptad motif of conserved amino acid residues in each peptide's primary amino acid sequence. Lennox expressly states that

repeated heptad motifs having appropriate amino acid sequences direct the HSP1 and HSP2 polypeptides to assemble into a heterodimeric  $\alpha$ -helical coiled-coil structure under permissible conditions. The individual  $\alpha$ -helical peptides contact one another along their respective hydrophobic faces, defined as the a and d positions of each heptad. Col. 6, lines 44-50.

The hydrophobic heptad binding described by Lennox et al. differs fundamentally from the binding of a "capture binding ligand comprising a nucleic acid." Nucleic acids bind complementary nucleic acids via hydrogen bonds between complementary bases, and do not depend on hydrophobic binding of heptad repeats. Changing an HSP1 peptide with a heptad repeat that binds similar heptad repeats by hydrophobic interactions to a capture binding ligand comprising a nucleic acid that binds complementary nucleic acids by hydrogen bonding thus fundamentally changes the principles operation of the cited reference.

Because "the proposed modification cannot change the principle of operation of a reference," the references are not sufficient to render the claims prima facie obvious.

# 4. The cited references fail to suggest that modifying their teachings would have a reasonable chance of success.

The references as a whole fail to provide a reasonable chance of success for making "a capture binding ligand comprising a nucleic acid, wherein the capture binding ligand is covalently bound to an electrode." No teaching of the claimed subject matter is made in any of the cited references, and as such the cited references fail to provide a reasonable expectation of success to make the claimed invention.

For all the reasons cited above, The cited references in combination fail to render the claims obvious. Applicants respectfully request that this ground for rejection be withdrawn.

#### Conclusion

Applicants submit the claims are in condition for allowance, and notification of such is respectfully requested. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,

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